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EDITORIAL

WILEY

A second case of multisystem inflammatory syndrome associated with SARS-CoV-2 in a liver-transplanted child

To the editor,

We read Petters et al.'s case report of a 3-year-old liver transplant recipient with multisystem inflammatory syndrome in children (MIS-C) with great interest.[1] Since MIS-C is a very rare complication of COVID-19, the probability of a child with liver transplant developing MIS-C should be extremely low. We present another case of MIS-C in a liver transplant recipient, that of a 5-year-old boy of Comorian origin, with NBAS deficiency who received a reduced deceased donor transplant at the age of 2 years (previously reported in Chavany et al.[2]). He developed hepatic artery thrombosis postoperatively and EBV-related lymphoproliferative disease, which resolved after immunosuppression was decreased. He was on tacrolimus monotherapy at presentation and was admitted to the emergency department for fever (39°C) with abdominal pain and non-bloody diarrhea. Initial laboratory tests showed inflammatory syndrome (C reactive protein (CRP), 58 mg/L; fibrinogen, 5.64 g/L; white blood cells, 6.8 G/L; neutrophils, 4.5 G/L; lymphocytes, 1.4 G/L) and normal hepatic function and enzymes. Fever persisted for 6 days with headaches, asthenia, anorexia, abdominal pain, vomiting, and diarrhea. Ultrasound imaging on hospital days 1 and 5 showed a thickening of the terminal ileum with multiple mesenteric nodes. On day 3, CRP levels had increased up to 247 mg/L, ferritin was at 500 µg/L, triglyceride levels were normal (1.4 mmol/L). He had transient lymphopenia (0.7 G/L). He developed renal failure, with a nadir creatinine level on day 4 of 47 µmol/L (Schwartz creatinine clearance, 63 mL/min) and urea at 10.4 mmol/L with a normal therapeutic tacrolimus level. He also had mildly increased liver enzymes on day 5 which normalized spontaneously. He was treated empirically by triple antibiotic therapy: ceftriaxone for 7 days, metronidazole for 5 days, and amikacin for 2 days. His status improved on day 6 with resumption of feeding and gastrointestinal function. Chest X-ray, electrocardiogram and cardiac ultrasonography results were all

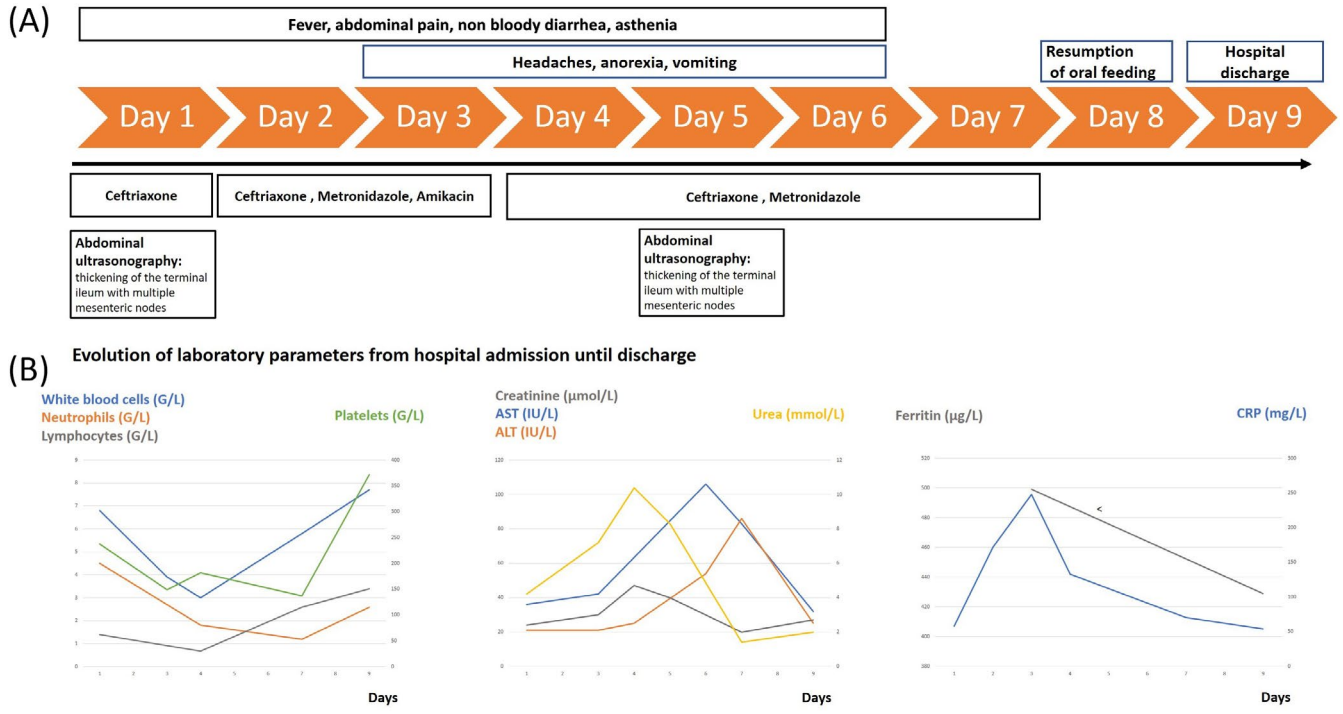

FIGURE 1 Timeline of key clinical events with associated laboratory evidence of inflammation during the patient's hospital stay Timeline. (A): Timeline of key clinical events, (B) laboratory evidence of inflammation during the patient's hospital stay

Abbreviations: ALT, Alanine transaminase; AST, Aspartate aminotransferase; CRP, C-reactive protein; ESR, Erythrocyte sedimentation rate; MIS-C, Multisystem inflammatory syndrome in children.

normal. Etiological investigations were negative. Specific anti SARS-CoV-2 IgG antibodies were detected. He had been in contact six weeks earlier with a person who had COVID-19 and had rhinitis for 48 h the following week. Our patient, therefore, met the CDC case definition for MIS-C: 5 years of age, fever, elevated inflammatory markers, clinically severe illness requiring hospitalization with organ involvement (renal and gastrointestinal), no plausible alternative diagnoses, COVID-19 exposure, and SARS-CoV-2 positive serology (82 AU, N<1). The diagnosis was made on day 6, when the patient's condition had improved, therefore, he received no immunoglobulin or steroid treatment, and there was no cardiac involvement. At 2 weeks' follow-up, clinical examination and laboratory findings were normal (normal liver enzyme levels, CRP at 8 mg/L). We thought that NBAS deficiency may have been a risk factor, but the case reported by Petters et al. suggests that MIS-C can occur in patients with other liver conditions. The similarities between the two cases are the patients' non-European ancestry (African-American and Comorian), which has been linked to an increased risk of MIS-C,[3] their gastrointestinal symptoms and mild COVID-19 course, which may have been a consequence of immunosuppressive therapy. Given that there are about 1200 liver-transplanted children in France (https://rams.agence-biomedecine.fr/greffe-hepatique-pediatrique-0), and that the current seroprevalence of SARS-CoV-2 antibodies in France is about 20%,[4] even one case would represent an approximately 20-fold higher risk than expected (about 1/250 versus 1/5000).[5] We cannot rule out that our case and Petters et al.'s are simply random occurrences but pediatric hepatologists should be aware of a possibly increased risk of MIS-C in liver-transplanted children. An international investigation should be conducted to assess this risk. Figure 1.

KEYWORDS

congenital liver disease, multisystem inflammatory syndrome, pediatric liver transplantation, SARS_CoV_2

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

Duvant Pauline: Case design and writing. Roquelaure Bertrand: Case design. Morand Aurélie, Bosdure Emmanuelle, Garaix Florentine, and Zandotti Christine: Article review. Fabre Alexandre: Case design and supervision.

DATA AVAILABILITY STATEMENT

Based on medical case, data are not available for public.

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